



## CASE CONFERENCE

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### CASE 2—1994 Management of a Cardiac Pheochromocytoma in Two Patients

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#### Case 1\*

A 41-year-old 70-kg woman presented with a history of headache, palpitations, and hypertension. The diagnosis of pheochromocytoma had been made 18 years previously on the basis of elevated plasma and urinary catecholamines. At that time, an exploratory laparotomy resulted in the excision of the left adrenal gland, which showed no pheochromocytoma. Her symptoms and blood pressure were well controlled following surgery, using alpha-methyl-*p*-tyrosine (AMPT) and propranolol, and no further investigations were performed. Further symptoms 6 months prior to this admission prompted investigation using metaiodobenzylguanidine (MIBG) scans in an attempt to localize the tumor. Two initial <sup>131</sup>I MIBG scans were negative but a <sup>123</sup>I MIBG scan suggested an abnormal focus in the right adrenal gland. AMPT was discontinued and phenoxybenzamine added to her treatment regimen before surgery. An uneventful laparotomy was performed to remove the remaining adrenal gland but again histology proved negative. Further laboratory investigations still demonstrated elevated plasma and urinary catecholamines (Table 1). Positron emission tomography and rapid-sequence contrast-enhanced computerized axial tomography (dynamic computed tomography [CT] scanning) demonstrated a 6 cm diameter mass in the region of the left atrium. The patient was scheduled for thoracotomy. Routine hematology, biochemistry, chest radiography, and a 12-lead electrocardiogram were normal. A surface echocardiogram was normal but a preoperative transesophageal echocardiogram confirmed the presence of the left atrial mass and demonstrated normal left ventricular function.

Antihypertensive medication 48 hours prior to surgery was as follows: phenoxybenzamine, 40 mg orally four times a day; propranolol, 20 mg orally four times a day; and nifedipine slow release, 10 mg orally twice a day. The heart rate (HR) was 80 to 90 beats/min and blood pressure (BP) 140/90 to 160/100 mmHg supine, 90/50 mmHg on standing (arm cuff and auscultation of the brachial artery). The usual doses of antihypertensive medication were given on the morning of surgery. Oral lorazepam, 2 mg, and intramuscular morphine, 8 mg, scopolamine, 0.2 mg, and hydrocortisone, 100 mg, were given as premedication. Before induction of anesthesia, two 14-g peripheral intravenous catheters,

a 20-g right radial arterial catheter, and a balloon-tipped, flow-directed, pulmonary artery catheter (via the right internal jugular vein) were inserted. A triple-lumen catheter was also inserted in the right internal jugular vein for intravenous vasoactive drug infusions. The patient remained adequately sedated before induction and hemodynamically stable on arrival in the preoperative holding area. However, after insertion of the arterial line the HR rose to 110 beats/min. Sinus rhythm and the invasive arterial BP were measured at 190/115 mmHg. Labetolol, 7.5 mg intravenously (IV), in divided doses of 2.5 mg, reduced the HR to 80 beats/min and BP to 170/100 mmHg.

Immediately before induction, the HR was 110 beats/min and BP 190/110 mmHg; esmolol (200 µg/kg/min reducing to 20 µg/kg/min after 5 minutes) and sodium nitroprusside (1.0 µg/kg/min) reduced the HR to 80 beats/min and BP to 150/70 mmHg. Anesthesia was induced using fentanyl (1 mg), 50% nitrous oxide in oxygen, thiamylal, 200 mg, followed by 2% isoflurane. Muscle relaxation was achieved using vecuronium (10 mg) and the patient's trachea was intubated without difficulty. Anesthesia was maintained using 50% nitrous oxide in oxygen, 1% isoflurane, and incremental fentanyl (total 2 mg); muscle relaxation was maintained using a vecuronium infusion (6 to 8 mg/hr). The arterial carbon dioxide tension was maintained between 30 to 40 mmHg. The HR remained 60 to 90 beats/min and BP 120/60 to 150/100 mmHg during intubation, skin incision, sternotomy, and aortic cannulation; the pulmonary artery pressure remained less than 25/12 mmHg during the pre-cardiopulmonary bypass (CPB)

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**Table 1. Plasma Catecholamine Levels Before Thoracic Surgery (Case 1)**

Catecholamine	Plasma Level (pg/mL)	Normal Range (pg/mL)
Norepinephrine	5,793	0-500
Epinephrine	121	0-100
Dopamine	3,918	0-100

period. Control of HR was achieved using esmolol (10 to 20  $\mu\text{g}/\text{kg}/\text{min}$ ) throughout the pre-CPB period, and BP using 2% isoflurane and nitroprusside (0–0.3  $\mu\text{g}/\text{kg}/\text{min}$ ). There was one episode of transient hypotension (60 mmHg systolic) during insertion of the venous bypass cannula and one episode of transient hypertension (200 mmHg systolic for 1 minute) during manipulation of the tumor mass before CPB. During CPB at 28°C, pump flows of 2 to 2.4 L/min/m<sup>2</sup> were maintained with a hematocrit of greater than 15%. Mean systemic BP was maintained between 40 and 70 mmHg using small increments of phenylephrine (50 to 100  $\mu\text{g}$ ).

A sessile tumor, approximately 5 cm in diameter, was found within the left atrium and attached to the posterior wall. The tumor mass encroached upon all four orifices of the pulmonary veins. The distal aortic arch was temporarily divided to obtain surgical access. The tumor and adjacent left atrium, including the distal pulmonary veins, were excised completely. The atrial defect was repaired using a large patch of pericardium and the four pulmonary veins were anastomosed to the patch. Total time spent on CPB was 322 minutes.

Hypotension during weaning from CPB (BP 65/35 mmHg) was due to a mild reduction in cardiac output (CO) (3.8 L/min), measured by thermodilution, and low calculated systemic vascular resistance (SVR) of 735 dynes  $\cdot$  sec  $\cdot$  cm<sup>-5</sup>. This was treated with volume infusion and dobutamine (5  $\mu\text{g}/\text{kg}/\text{min}$ ) to restore CO to greater than 4.5 L/min. Norepinephrine (0.1 to 0.2  $\mu\text{g}/\text{kg}/\text{min}$ ) was added to maintain BP at greater than 100 mmHg systolic (Table 2). Intraoperative transesophageal echocardiography (Sonos 1000, Hewlett Packard, Palo Alto, CA) assisted in the estimation of left ventricular filling volume and contractility by comparing views of the pre-CPB and post-CPB periods. Left ventricular ejection fraction was formally calculated only during the pre-CPB period (approximately 55%); post-CPB images of the left ventricle were then compared directly with the pre-CPB image as an assessment of filling and contractility. During weaning, qualitative echocardiographic assessment revealed decreased left ventricular filling and the requirement for volume administration. Comparative values for BP, CO, and SVR during the preinduction, pre-CPB, and post-CPB periods are given in Table 2.

At the end of surgery the patient was transferred to the cardiothoracic intensive care unit, intubated, and ventilated. She remained hemodynamically stable but returned to the operating room after 4 hours because of excessive bleeding from the chest drains; a small arterial bleeding point in the left atrium was found and secured. Weaning off dobutamine and norepinephrine was accomplished on the

second postoperative day and the patient was extubated on the third postoperative day. Small doses of oral captopril and propranolol were required in the first 10 days following extubation to control blood pressure and heart rate.

The patient was maintained on hydrocortisone, 100 mg every 6 hours, throughout the perioperative period commencing with the premedication; a further 100 mg was given intraoperatively just prior to the termination of CPB. In the postoperative period the dose of hydrocortisone was reduced and weaned following extubation. The patient was finally discharged from the hospital 3 weeks after surgery on steroid replacement therapy and no antihypertensive therapy (BP 130/90 mmHg supine). Histologic analysis of the surgical specimen confirmed the diagnosis of pheochromocytoma.

#### Case 2†

The patient was a 27-year-old, 75-kg, Egyptian woman with a 6-month history of hypertension and diaphoresis. After an extensive work-up she was found to have an unresectable, intracardiac pheochromocytoma that was isolated to structures of the left heart. She was transferred to this institution for consideration for orthotopic heart transplantation. The patient had no symptoms of dyspnea, chest pain, pulmonary edema, or heart failure. There was no history of drug allergies. Her current medications included propranolol and dibenzylamine. Her medical history was otherwise noncontributory. She was deemed an acceptable transplant candidate.

A suitable donor heart was eventually procured. The patient was brought to the operating room, anxious, but without any specific complaints. She had eaten a solid meal 2 hours prior to arrival in the operating room. Her heart rate was 98 beats/min, BP 148/95 mmHg, 100% O<sub>2</sub> saturation by pulse oximetry, and sinus rhythm without conduction defect on the electrocardiogram. Two large-bore peripheral intravenous catheters and an intra-arterial monitoring catheter were inserted. The patient was administered oxygen, 5 L/min via nasal cannula, and midazolam, 2 mg, was administered intravenously. A pulmonary artery catheter was then inserted and revealed the following: PAP 28/9 mmHg, central venous pressure (CVP) 5 mmHg, and cardiac output 6.8 L/min. During the insertion of the catheter, the patient was given propranolol, 3 mg IV in divided doses, in order to control her HR between 95 and 105 beats/min and an additional dose of midazolam, 3 mg IV, to allay her anxiety. After preoxygenation with 100% O<sub>2</sub> for 5 minutes, rapid-sequence induction, and intubation of the trachea using cricoid pressure were easily accomplished with sodium thiopental, 500 mg, fentanyl, 2 mg, lidocaine, 100 mg, and vecuronium, 14 mg. Intravenous lidocaine was used to attenuate a possible increased hemodynamic response to laryngoscopy and intubation. At this time, the BP rose to 196/90 mmHg and the HR remained stable between 90 and 100 beats/min. Following tracheal intubation, a 5-MHz biplane transesophageal echocardiography (TEE)

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**Table 2. Case 1: Comparison of Representative Hemodynamic Parameters and Treatment at Four Different Times During the Perioperative Period**

	Preinduction	Pre-CPB	Weaning CPB	Post-CPB
Heart rate (beats/min)	110	80	90	90
Blood pressure (mmHg)	190/110	140/90	65/35	105/55
CVP (mmHg)	7	9	10	10
PAP (mmHg)	22/6	24/12	30/14	28/15
Cardiac output (L/min)	6.0	5.8	3.8	5.0
Cardiac index (L/min/m <sup>2</sup> )	3.2	3.2	2.1	2.7
SVR* (dynes·sec·cm <sup>-5</sup> )	1730	1340	735	990
Treatment	Labetolol Nitroprusside Esmolol	Anesthesia Nitroprusside Esmolol	Volume Dobutamine Norepinephrine	Dobutamine Norepinephrine

Abbreviations: CVP, central venous pressure; PAP, pulmonary artery pressure; SVR, systemic vascular resistance.

\*SVR = 80 (mean systemic blood pressure – central venous pressure/cardiac output). Normal range: 900 to 1,500 (dynes·sec·cm<sup>-5</sup>).<sup>38</sup>

probe was inserted into the esophagus and attached to a Hewlett-Packard Sonos 100 machine. A mass measuring approximately 8 cm by 5 cm was seen anterolateral to the aortic root and left ventricle. This mass compressed the left atrium and extended to the mid-left ventricular level. It appeared to be well delineated without extension into the cardiac chambers. The short-axis view revealed no evidence of left ventricular hypertrophy or dyskinesis. None of the valves was involved (Fig 1).

General anesthesia was maintained with oxygen, fentanyl, isoflurane, and vecuronium. In addition to deepening anesthesia, nitroprusside was used to treat intermittent systolic blood pressure elevations of 150 to 180 mmHg. During these acute hypertensive episodes, the TEE revealed a hyperdynamic left ventricle without evidence of wall motion abnormalities. Arterial blood gas determinations were monitored serially and urinary output was measured at 30-minute intervals. A median sternotomy was performed and the operative course was unremarkable prior to CPB and aortic cross-clamping. The tumor was poorly encapsulated and demonstrated such extensive invasion of the walls of the left atrium and ventricle that complete removal could not be achieved with full thickness excision and pericardial patch grafting. The patient underwent cardiac allotransplantation and was weaned from cardiopulmonary bypass on isoproterenol (0.1 mg/min) and dopamine (3 µg/kg/min), requiring only a brief period of norepinephrine (0.05 µg/kg/min) administration immediately following CPB to maintain systolic BP greater than 100 mmHg. Cardiac output determinations following CPB ranged from 6.9 to 8.8 L/min. She was transferred to the ICU in stable condition and was extubated uneventfully on the second postoperative day. There was no recurrence of her hypertension and her only medications upon discharge were acyclovir, cyclosporine, and vitamins.

#### DISCUSSION†

Pheochromocytomas are rare catecholamine-secreting tumors found in approximately 0.1% of all hypertensive patients.<sup>1</sup> Approximately 18% of all pheochromocytomas

are extra-adrenal,<sup>2</sup> with 75% of extra-adrenal tumors located between the diaphragm and the aortic bifurcation. Less than 2% of all pheochromocytomas are intrathoracic; middle mediastinal tumors of the heart and pericardium are even rarer with the tumor mass usually related to the left atrial wall.<sup>3</sup> Although the diagnosis and surgical management of thoracic pheochromocytomas requiring CPB have been described previously,<sup>3-6</sup> a description of the anesthetic technique did not appear in the literature.

Localization of intrathoracic pheochromocytomas may be difficult, resulting in multiple investigations and negative laparotomy.<sup>4</sup> In a review of the surgical literature, Jebara et al<sup>6</sup> found only 30 reported cases of intracardiac pheochromocytomas during an 18-year period. Most cases had been reported in the past 6 years, suggesting an improvement in the diagnostic techniques available.

Rapid-sequence intravenous contrast computerized axial tomographic scanning (dynamic CT scanning) and <sup>131</sup>I MIBG scanning (with blood-pool and skeletal imaging) have been described as effective techniques in the localization of these tumors.<sup>4</sup> Scintigraphy using <sup>131</sup>I MIBG may be particularly helpful in patients with recurrent disease if used in association with other techniques such as magnetic resonance imaging and computerized axial tomography. Maurca et al<sup>7</sup> compared these three techniques, reporting a sensitivity of 83% and a specificity of 100% for <sup>131</sup>I MIBG scanning in patients with extra-adrenal or malignant tumors. It has been suggested that <sup>123</sup>I MIBG may be superior to <sup>131</sup>I MIBG scanning in patients with neural crest tumors.<sup>8</sup> Case 1 was unusual in that <sup>131</sup>I MIBG and <sup>123</sup>I MIBG scanning were both misleading, suggesting a tumor in the remaining adrenal gland. This tumor was finally localized to the left atrium using dynamic CT scanning and <sup>11</sup>C-labeled hydroxyephedrine positron emission tomography. The latter technique has been described by Shulkin et al.<sup>9</sup> The imaging techniques used for the localization of pheochromocytomas have been recently reviewed by Chatal.<sup>2</sup>

Inhalation, intravenous, and regional anesthetic techniques have all been used successfully in the management of patients with pheochromocytomas.<sup>10</sup> The importance of adequate preoperative hemodynamic control (blood pressure, arrhythmias, blood volume) before surgery has been

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**Fig 1. Case 2. (A) A modified five-chamber view of the heart using the horizontal probe. This demonstrates the mass anterolateral to the aortic root. Abbreviations: AV, aortic valve; LA, left atrium; RA, right atrium; RV, right ventricle. (B) A two-chamber view using the vertical plane. This demonstrates the mass in the pericardium anterior to the LV. Abbreviation: MV, mitral valve.**

described by a number of authors.<sup>1,11-13</sup> Alpha-methyl-tyrosine inhibits tyrosine hydroxylase and blocks the rate-limiting conversion of tyrosine to dopa in the catecholamine synthesis pathway.<sup>1</sup> AMPT may be particularly useful in patients with malignant pheochromocytomas, or in those for whom surgery is contraindicated.<sup>14</sup> However, a tumor partially suppressed by AMPT may still cause major pressor responses during surgery; the addition of an  $\alpha$ -adrenoreceptor antagonist is essential and phenoxybenzamine remains the drug of choice.<sup>1</sup> Satisfactory preoperative hemodynamic control was achieved in Case 1 using oral phenoxybenzamine, propranolol and nifedipine; these drugs were given up to and including the morning of surgery. The combination of lorazepam, morphine, and scopolamine has been recommended as premedication for patients with pheochromocytoma,<sup>15</sup> although other authors have suggested that morphine should be avoided because of histamine-induced

catecholamine release.<sup>1,12</sup> Atropine premedication, if it is given at all, should be given with caution to pediatric pheochromocytoma patients because of its chronotropic effects.<sup>12</sup> Although patient 1 was adequately sedated and initially hemodynamically stable after premedication, the first direct arterial BP reading before induction of anesthesia was 190/115 mmHg.

It was anticipated that large doses of anesthetic agents, nitroprusside, and a  $\beta$ -adrenoreceptor antagonist might be required to control fluctuations in HR and BP in the period before CPB, especially during exploration of the mediastinum and manipulation of the heart. Nicholas et al<sup>16</sup> used a propranolol bolus (3 mg IV) followed by esmolol (up to 300  $\mu$ g/kg/min) and sodium nitroprusside for hemodynamic control during laparotomy for pheochromocytoma resection. Gabrielson et al<sup>17</sup> used esmolol (up to 250  $\mu$ g/kg/min without an initial bolus) and phentolamine without cardio-

pulmonary bypass. Isoflurane and sodium nitroprusside were used as the primary agents to control hypertension; esmolol was then titrated to maintain a heart rate of less than 80 beats/min. There is some evidence that the elimination of esmolol is slightly prolonged in anesthetized patients receiving chronic  $\beta$ -blocking agents; this effect is unlikely to be clinically important and the dosage of esmolol can be titrated to individual effect.<sup>18</sup> In Case 1, esmolol was maintained at the relatively low infusion rate of 10 to 20  $\mu\text{g}/\text{kg}/\text{min}$ , following the initial infusion of 200  $\mu\text{g}/\text{kg}/\text{min}$  during induction of anesthesia.

Boluses of labetalol (7.5 mg in total) were used to control both tachycardia and hypertension immediately before induction of anesthesia. The greater duration of action of labetalol, compared to esmolol, was useful during the period while the patient was moved from the preoperative area to the operating room. It has been suggested that intravenous labetalol, which is predominantly a  $\beta$ -blocker, may give unreliable responses when used in patients with pheochromocytoma.<sup>17</sup> In the authors' experience it may be used under these circumstances, primarily to control heart rate and thus reduce hypertension, in conjunction with preexisting alpha blockade (usually phenoxybenzamine).

There are little data concerning the pharmacodynamics of  $\beta$ -adrenoreceptor antagonist drugs before, during, and after CPB. In human subjects, plasma propranolol levels drop after the onset of hypothermic CPB but rise again after the termination of CPB.<sup>19,20</sup> A peak in plasma propranolol levels occurs during rewarming on CPB in dogs.<sup>21</sup> Esmolol is an ultra-short-acting  $\beta_1$ -adrenoreceptor antagonist with a rapid onset of action and rapid metabolism to a metabolite which is 1,500 times less potent than esmolol itself.<sup>22</sup> In Case 1 esmolol was selected to minimize the effects of residual beta-adrenergic blockade during weaning from CPB. Hypotension at this time was due to a low systemic vascular resistance and depression of cardiac output due primarily to a reduction in preload. Hypotension has been reported previously following resection of pheochromocytoma and is thought to be due to residual alpha-adrenergic blockade and fall in plasma catecholamine levels after tumor resection.<sup>1</sup> The simultaneous measurement of CO, systemic BP, and central venous pressure following CPB allowed SVR to be calculated and kept within the normal range using norepinephrine.

Cardiomyopathy has been reported to be present in 20% to 30% of patients with pheochromocytoma.<sup>23</sup> In Case 1, there was no echocardiographic evidence of preoperative left ventricular dysfunction. Low cardiac output syndrome following cardiopulmonary bypass may be due to a number of factors including arrhythmias, decreased preload, volume overload, increased afterload, and myocardial dysfunction.<sup>24</sup> In Case 1 there was no echocardiographic evidence of ventricular dysfunction during the intraoperative period and the mild reduction in CO postbypass was secondary to a decrease in preload demonstrated by serial qualitative echocardiographic assessment. The simultaneous increase in SVR, using norepinephrine, may also have improved coronary arterial perfusion and ventricular function.

Hemodynamic dysfunction related to the presence of an atrial mass was a further consideration. Atrial myxomas are the most common primary tumor of the heart. These tumors may cause atrial arrhythmias, obstruct left atrial outflow (in which case central venous and pulmonary capillary wedge pressure will no longer reflect left ventricular end-diastolic pressure), embolize fragments of tumor or release vasoactive substances (particularly vasoactive intestinal polypeptide [VIP]).<sup>25</sup> A pulmonary artery catheter should be avoided in the presence of a right atrial mass. This potential list of problems may all have been encountered in the reported cases. In particular, tachycardia and tachyarrhythmias due to acidosis, electrolyte imbalance, and inotropic agents were avoided.

The commonest serious postoperative complication and cause of mortality in patients undergoing surgical resection of cardiac pheochromocytoma is massive bleeding. Jebara et al<sup>6</sup> reported 25 cases of patients undergoing surgical resection of a cardiac pheochromocytoma: there were 21 survivors, 20 of whom were reported to be completely cured. All 4 deaths were due to massive bleeding shortly after surgery. Case 1 returned to the operating room after 4 hours following excessive bleeding from the chest drains.

Finally, the relationship between pulmonary capillary wedge pressure and left atrial pressure or left ventricular end-diastolic volume may be poor following CPB.<sup>26</sup> In Case 1 it was anticipated that distortion of the left atrium and pulmonary veins, following surgical repair, might further limit the value of pulmonary arterial monitoring to estimate left ventricular filling. Measurement of direct left atrial pressure in this case may have proved useful. In fact, during weaning from CPB it was found that echocardiographic changes in left ventricular function (filling and contractility) were paralleled by similar changes in pulmonary artery diastolic pressure, CO, and systemic BP.

To summarize, a number of important issues should be considered in the management of these rare cases: these include difficulty in preoperative tumor localization, adequate preoperative control of hemodynamic variables, intraoperative hemodynamic fluctuation due to catecholamines or the presence of an atrial mass, a low SVR following tumor resection, and the possibility of massive blood loss in the immediate postoperative period.

#### COMMENTARY§

The report of these two patients presenting with cardiac pheochromocytoma is noteworthy for multiple reasons. First, these cases illustrate many of the current and advanced diagnostic techniques used for identifying pheochromocytomas. Second, various combinations of  $\beta$ -adrenergic blockers and vasodilators were used effectively to control the hemodynamic derangements. Lastly, and perhaps most importantly, there is a presentation for the first time in the anesthesia literature of a detailed description of the care of two patients with cardiac pheochromocytomas.

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The first patient is a 41-year-old woman who underwent two unsuccessful adrenalectomies to resect a symptomatic pheochromocytoma. Ultimately, a left atrial tumor was diagnosed using PET scanning, dynamic CT, and finally transesophageal echocardiography. Surgical resection was planned using cardiopulmonary bypass. The second patient is a 27-year-old woman who was found to have an unresectable intracardiac tumor after an extensive workup. She was scheduled for cardiac transplantation, also with CPB. Even without the tumors secreting vasoactive amines, these cases would present many complex anesthetic problems. Superimposed upon this, secretion of these vasoactive compounds evokes the real possibility of sudden and profound hemodynamic changes that must be dealt with. Medications used to control hypertension may substantially increase the difficulty in weaning from CPB.<sup>17</sup> Thus, particular attention must be paid to their choice, and short-acting agents are preferred.

The first patient was managed intraoperatively with labetalol and esmolol for beta-adrenergic blockade and with sodium nitroprusside (SNP) added as a potent vasodilator, as is recommended for rapid and precise titration of blood pressure.<sup>28</sup> Esmolol alone may have sufficed here for beta-blockade<sup>17</sup>; however, the combination of a longer acting agent with a very short duration one may have some merit in "smoothing out the course." The second case was managed intraoperatively with small doses of propranolol in combination with SNP again for rapid and precise control of BP and heart rate. She had received prior alpha-adrenergic blockade with the long-acting blocker, dibenzylamine, which, along with intravascular volume expansion, remains the mainstay of therapy here.<sup>29,30</sup>

It is unfortunate that only from numerous case reports can a better picture of this disease be obtained. Numerous anecdotal reports (too numerous to mention) have confirmed the safety or danger of various drugs used in this condition. The current mortality from surgical resection of this tumor intraabdominally is quite low.<sup>31</sup> What remains are problems with special situations such as pheochromocytoma that are previously undiagnosed,<sup>32</sup> occur in pregnancy,<sup>33</sup> or are located in extra-adrenal sites such as the heart.<sup>3</sup> With this report there is now the beginning of a picture of problems associated with management of cardiac pheochromocytoma.

These cases remind me of a similar one that I cared for not too long ago. A middle-aged man who had previously undergone cardiac transplantation now presented for a resection of an intraabdominal pheochromocytoma. The actions of various anesthetic and vasoactive medications used in the treatment of pheochromocytoma had to be scrutinized for use in the denervated heart. This was more than a novelty case or a worse-case scenario board-examination question. It represented a challenging pharmacologic exercise for even the most experienced anesthesiologist, and one I will long remember. The cases presented here are likewise superb examples of challenging clinical and academic exercises for all to share.

#### COMMENTARY

Extra-adrenal pheochromocytomas are rare. They are usually located in the abdomen. Thoracic pheochromocytomas constitute 1% to 2% of all cases of pheochromocytomas and are usually found in the posterior mediastinum. Cardiac pheochromocytomas are extremely rare, with fewer than 50 cases reported in the literature.<sup>6</sup> Diagnosis and management of these tumors constitute a challenging problem to both the medical and the surgical team.

Diagnosis of cardiac pheochromocytomas is consistently difficult to establish. In most instances, multiple investigative procedures are performed in different combinations over several years before the site of the lesion is localized. Furthermore, during the diagnostic workup, negative exploratory laparotomy was performed in over half of the cases,<sup>6</sup> two of whom died postoperatively.<sup>34,35</sup> The most useful study to establish the diagnosis of cardiac pheochromocytoma is iodine 131-labeled metaiodobenzyl guanidine (I-MIBG) scintigraphy.<sup>4</sup> This technique resulted in localization of the tumor in 18 of the 22 patients in whom it was used.

Two-dimensional echocardiography is particularly helpful when the tumor has an intracardiac extension. The CT scan had a very low diagnostic yield because it was performed in most cases and revealed the diagnosis in only one patient. However, after the diagnosis had been established using another technique, retrospective analysis of the CT scan showed the exact location of the tumor. Recently, rapid-sequence contrast-enhanced CT scan (dynamic CT) proved to be promising in the diagnosis of cardiac pheochromocytomas. Magnetic resonance imaging (MRI), with its superior soft-tissue contrast, appears to be a modality with great diagnostic potential. However, as with dynamic CT, experience with these two techniques is very limited. Moreover, in the rare cases where it was obtained, MRI did not help establish the diagnosis. As with the CT scan, retrospective analysis of the MRI images after the diagnosis had been made allowed visualization of the tumor.

Pheochromocytomas are most often found on the roof of the left atrium. Other locations include the interatrial septum and the anterior surface of the heart between the aortic root and the pulmonary artery with possible posterior extension. Coronary angiography is a valuable procedure because it shows the exact location of the tumor as well as its relation to the coronary vessels. It also indicates the origin of the blood supply of the pheochromocytoma and helps in the planning of the surgical procedure.

Surgical excision of these tumors offers permanent cure. However, careful anesthetic preparation is mandatory before the operation. An important characteristic feature of resection of cardiac pheochromocytomas is the use of cardiopulmonary bypass. This allows total exclusion of the heart after cardioplegic arrest with the aorta cross-clamped and both vena cavae snared. Unlike other extracardiac locations, the tumor can then be excised without risk of

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hypertension or arrhythmias and with minimal blood loss. Furthermore, aortic cross-clamping allows safe dissection of the mass from the underlying myocardium and from the coronary vessels. It also allows the performance of coronary artery procedures to completely excise the mass. In some cases a segment of the left atrial wall containing the tumor is resected and replaced by a pericardial or Dacron patch.

Some authors advocate transection of the great vessels to obtain access to pheochromocytomas of the roof of the left atrium.<sup>36</sup> Cooley et al<sup>37</sup> in 1985 described a new surgical approach to treat extensive tumors involving the posterior surface of the heart: cardiac autotransplantation after complete excision of the mass. Surgical resection of cardiac pheochromocytomas carries a high operative mortality because among the 25 patients who underwent surgical resection 4 died (16%). All four deaths were due to massive bleeding and occurred either intraoperatively or shortly after the operation. Moreover, nonlethal hemorrhagic complications were encountered in 4 other patients so that 8 of 25 patients (32%) presented serious postoperative bleeding from the tumor bed.

The two cases reported by Lewis et al and Mullis et al illustrate perfectly the different aspects and problems encountered in the management of cardiac pheochromocytomas. Difficulties in posing the diagnosis and in localizing the tumor were clearly demonstrated in both cases. In Case 1 two negative laparotomies were performed with ablation of two normal adrenal glands in an 18-year interval before the cardiac tumor could be discovered. The use of rapid-sequence contrast-enhanced CT scan and PET were of great help in localizing the tumor.

The tumor sites were characteristic of cardiac pheochromocytomas because both tumors involved the left atrium with extension into the left ventricular structures in Case 2. Also illustrated in these two papers is the difficulty in the surgical management. In Case 1 resection of the tumor required a large resection of the left atrium and reimplantation of all the pulmonary veins. This is an unusual proce-

dure necessitating high surgical expertise. In this case, as in one third of the cases in the literature, postoperative bleeding occurred, requiring reoperation.

In Case 2 the massive extension of the tumor to the left ventricle precluded total resection, and orthotopic heart transplantation was performed with success. This is a very impressive case, the first published in the world literature. Although heart transplantation may seem a high price to pay for cardiac pheochromocytomas, it might be a necessary operation when extensive involvement of the heart or of the main coronary vessels is encountered. In these cases, incomplete resection results in recurrence of symptoms, whereas total ablation may result in uncontrollable bleeding and/or ischemia and death.

Difficulty in resection is usually due either to difficult exposure when the tumor is located on the posterior aspect of the heart or when involvement of crucial structures such as the main left coronary artery occur. Furthermore, cardiac pheochromocytomas are consistently poorly encapsulated and infiltrate adjacent structures. Several surgical techniques have been described to help overcome these difficulties including (1) transection of the aorta and pulmonary trunk offering better access to the roof of the left atrium and (2) removal of the heart and autotransplantation. Both of these techniques improve the exposure and allow better manipulation in the majority of cases; however, they do not constitute a radical solution when extensive cardiac involvement exists. In these rare cases orthotopic heart transplantation is probably the optimal choice. The most difficult issue in these situations is the ability to detect preoperatively the degree of extension of the tumor and its nonresectability in order to include the patient in a pretransplant program.

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#### REFERENCES

- Hull CJ: Pheochromocytoma. Diagnosis, preoperative preparation and anaesthetic management. *B J Anaesth* 58:1453-1468, 1986
- Chatal J: Can we agree on the best imaging procedure(s) for localization of pheochromocytomas? *J Nucl Med* 34:180-181, 1993
- David TE, Lenkei SC, Marquez-Julio A, et al: Pheochromocytoma of the heart. *Ann Thorac Surg* 41:98-100, 1986
- Shapiro B, Sisson J, Kalff V, et al: The location of middle mediastinal pheochromocytomas. *J Thorac Cardiovasc Surg* 87:814-820, 1984
- Besterman E, Bromley LL, Peart WS: An intrapericardial pheochromocytoma. *B Heart J* 36:318-320, 1974
- Jebara VA, Uva MS, Farge A, et al: Cardiac pheochromocytomas. *Ann Thorac Surg* 53:356-361, 1992
- Maurea S, Cuocolo A, Reynolds JC, et al: Iodine-131-metaiodobenzylguanidine scintigraphy in preoperative and postoperative evaluation of paraganglioma: Comparison with CT and MRI. *J Nucl Med* 34:173-179, 1993
- Gelfand MJ, Paltiel HJ, Elgazzar AH, et al: I-123-MIBG imaging of neural crest tumors. *J Nucl Med* 33:1072, 1992
- Shulkin BL, Wieland DM, Thompson NW, et al: PET scanning with hydroxyephedrine: An approach to the localization of pheochromocytoma. *J Nucl Med* 33:1125-1131, 1992
- Strebel S, Scheidegger D: Propofol-fentanyl anesthesia for pheochromocytoma resection. *Acta Anaesth Scand* 35:275-277, 1992
- Roizen MF: Diseases of the endocrine system, in Katz J, Benumof JL, Kadis LB, (eds). *Anesthesia and Uncommon Diseases*. Philadelphia, Saunders, 1990, pp 267-279
- Pullerits J, Ein S, Williamson Balfe J: Anaesthesia for pheochromocytoma. *Canadian J Anaesth* 35:526-534, 1988
- Pratila V, Pratila MG: Anaesthetic management of pheochromocytoma. *Canadian Anaesth Soc J* 26:253-259, 1979
- Juan D: Pharmacologic agents in the management of pheochromocytoma. *South Med J* 75:211-216, 1982
- Stoelting RK, Dierdorf SF, McCammon RL: *Anesthesia and coexisting diseases*. New York, Churchill Livingstone, 1988, p 506

16. Nicholas E, Deutschmann CS, Allo M, Rock P: Use of esmolol in the intraoperative management of pheochromocytoma. *Anesth Analg* 67:1114-1117, 1988
17. Gabrielson GV, Guffin AV, Kaplan JA, et al: Continuous intravenous infusions of phentolamine and esmolol for preoperative and intraoperative adrenergic blockade in patients with pheochromocytoma. *J Cardiothorac Anesth* 1:554-558, 1987
18. de Bruijn NP, Reves JG, Croughwell N, et al: Pharmacokinetics of esmolol in anesthetized patients receiving chronic beta blocker therapy. *Anesthesiology* 66:323-326, 1987
19. Plachetka JR, Salomon NW, Copeland JG: Plasma propranolol before, during and after cardiopulmonary bypass. *Clin Pharmacol Ther* 30:745-751, 1981
20. Sill JC, Nugent M, Moyer TP, et al: Influence of propranolol levels on hemodynamics during coronary artery bypass surgery. *Anesthesiology* 60:455-463, 1984
21. McAllister RG, Bourne DW, Tan GT, et al: Effects of hypothermia on propranolol kinetics. *Clin Pharmacol Ther* 25:1-7, 1979
22. Fenner SG, Mahoney A, Cashman JN: Repair of traumatic resection of the thoracic aorta: Esmolol for intraoperative control of aortic pressure. *Br J Anaesth* 67:483-487, 1991
23. Gilanz FJ, Luengo C, Conjero P, et al: Cardiomyopathy and phaeochromocytoma. *Anaesthesia* 38:888-891, 1983
24. Comunale ME, Lisbon A: Postoperative care of the cardiac surgical patient, in DiNardo JA, Schwartz MJ (eds). *Anesthesia for cardiac surgery*. Norwalk, CT, Appleton and Lange, 1990, pp 313-326
25. Johns RA, Kron IL, Carey RM, et al: Atrial myxoma: Case report, brief review and recommendations for anesthetic management. *J Cardiovasc Anesth* 2:207-212, 1988
26. Hines R, Barash PG: Pulmonary artery catheterization, in Blitt CD (ed): *Monitoring in Anesthesia and Critical Care Medicine*. New York, Churchill Livingstone, 1990, pp 260-263
27. Shimosato S, Carter KG, Brom DH, Hiratzka L: Hypertensive crisis during coronary artery bypass graft surgery: A case of unsuspected pheochromocytoma. *J Cardiothorac Anesth* 1:318-320, 1987
28. Csanky-Treels JC, Lawick Van Pabst WPI, Brands JWJ, et al: Effects of sodium nitroprusside during the excision of phaeochromocytoma. *Anaesthesia* 31:60-62, 1976
29. Perry LB, Gould AB: The anesthetic management of pheochromocytoma: Effect of preoperative adrenergic blocking drugs. *Anesth Analg* 51:36-40, 1972
30. Gebbie DM, Finlayson DC: Use of alpha and beta adrenergic blocking drugs and halothane in the anaesthetic management of phaeochromocytoma. *Can Anaes Soc J* 14:39-43, 1967
31. Roisen MF, Schreider BD, Hassan SZ: Anesthesia for patients with pheochromocytoma, in MF Roisen (ed): *Anesthesia for Patients With Endocrine Disease*. *Anesthesiol Clin North Am* Saunders, Philadelphia, PA, 1987, pp 269-275
32. Brown P, Caplan RA: Recognition of an unsuspected phaeochromocytoma during elective coronary artery bypass surgery. *Can Anaesth Soc J* 33:785-789, 1986
33. Mitchell SZ, Freilich JD, Brandt D, et al: Anesthetic management of pheochromocytoma resection during pregnancy. *Anesth Analg* 66:487-480, 1987
34. Hodgson SF, Sheps SG, Subramanian R, et al: Catecholamine secreting paraganglioma of the interatrial septum. *Am J Med* 77:157-161, 1984
35. Geisler F, Barth G, Jaeck D, et al: Un cas de pheochromocytoma a localisation cardiaque. *Presse Med* 14:1024-1026, 1985
36. Besterman F, Bromley LL, Peart WS: An intrapericardial pheochromocytoma. *Br Heart J* 36:318-320, 1974
37. Cooley DA, Reardon MJ, Frazier OH, Angelini P: Human cardiac explantation and autotransplantation application in a patient with a large cardiac pheochromocytoma. *Tex Heart Inst J* 9:1103-1105, 1985
38. Reich D, Kaplan JA: Hemodynamic monitoring, in Kaplan JA (ed): *Cardiac Anesthesia*. Philadelphia, PA, Saunders, 1983, p 261-298